

04-04-2001

-31 -

EP 000005005

PCT/EP00/05005

2 April 2001

MediGene Aktiengesellschaft

M29186PCT BÖ/DLh/pvc

Deutsches Krebsforschungszentrum

Patent claims

1. T-cell epitope having an amino acid sequence AQIFNKPYW, AGVDNRECI, and/or a functionally active variant thereof.
2. T-cell epitope according to claim 1, characterized in that said variant has a sequence homology to AQIFNKPYW or AGVDNRECI of at least 65%, preferably at least 75% and in particular at least 85% at the amino acid level.
3. T-cell epitope according to claim 1, characterized in that said variant is structurally homologous to AQIFNKPYW or AGVDNRECI.
4. T-cell epitope according to any of claims 1-3, characterized in that the T-cell epitope is a cytotoxic T-cell epitope.
5. Compound comprising a T-cell epitope according to any of claims 1 to 4, wherein the compound is not a naturally occurring L1 protein, i.e. is a naturally occurring L1 protein which itself or whose nucleotide and/or amino acid sequence has been genetically modified, of a papillomavirus and not an exclusively N-terminal or an exclusively C-terminal deletion mutant of a naturally occurring L1 protein of a papillomavirus.
6. Compound according to claim 5, characterized in that the compound is a polypeptide, in particular a fusion protein.

AMENDED SHEET

7. Compound according to claim 5 or 6, characterized in that the compound is a polypeptide of at least 50 amino acids, preferably of at least 35 amino acids, in particular of at least 20 amino acids and particularly preferably of at least 10 amino acids, in length.
8. Compound according to any of claims 5-7, characterized in that the compound contains a chemical, radioactive, nonradioactive isotope and/or fluorescent label of the T-cell epitope and/or of said fusion protein, and/or a chemical modification of the T-cell epitope and/or fusion protein.
9. Nucleic acid, characterized in that it codes for a T-cell epitope or a compound containing a T-cell epitope according to any of claims 5-8.
10. Vector, in particular an expression vector, characterized in that it contains a nucleic acid according to claim 9.
11. Cell, characterized in that it contains, preferably presents, at least one T-cell epitope according to any of claims 5-8.
12. Cell according to claim 11, characterized in that the cell is transfected, transformed and/or infected with a nucleic acid according to claim 9 and/or a vector according to claim 10.
13. Cell according to claim 11, characterized in that the cell was incubated with at least one compound according to any of claims 5-8 and/or at least one complex according to any of claims 15-17 containing a T-cell epitope according to any of claims 5-8.

14. Cell according to claim 11 or 12, characterized in that the cell is a B cell, a macrophage, a dendritic cell, an embryonic cell, a fibroblast, a B16F10, a B6, a C3, an EL4, a RMA or a RMA-S cell.
15. Complex comprising a T-cell epitopes according to any of claims 1-4 or a compound according to any of claims 5-8 and at least one further compound.
16. Complex according to claim 15, characterized in that the complex contains at least one MHC class I molecule, preferably as H2-D^b tetramer.
17. Complex according to claim 16, characterized in that the said MHC class I molecule is a human or murine MHC class I molecule, in particular an MHC class I molecule derived from C57B1/6 mice.
18. Method for in vitro detection of the activation of T cells by at least one compound containing a T-cell epitope according to any of claims 1-4, which comprises the following steps:
- a) stimulation of cells using at least one said compound;
 - b) addition of at least one target cell presenting a T-cell epitope according to any of claims 1-4 or a complex according to any of claims 15-17, and
 - c) determination of T-cell activation.
19. Method according to claim 18, characterized in that it comprises, after step a), the following additional step a')):

a') coculturing of the cells for approx. 12 days, in particular at least 5 days, with:

(i) at least one target cell loaded with a compound according to any of claims 5-8, at least one complex according to any of claims 15-17, at least one capsomer, at least one stable capsomer, at least one VLP, at least one CVLP, and/or at least one virus,

(iii) at least one complex according to any of claims 15-17,

(iii) and/or at least one target cell presenting a T-cell epitope according to any of claims 1-4,

prior to step b).

20. Method for producing a target cell according to any of claims 11, 13, 14, 18 or 19, characterized in that the target cell is incubated with at least one compound according to any of claims 5-8 and/or at least one complex according to any of claims 15-17 containing a T-cell epitope according to any of claims 5-8.
21. Method for producing a target cell according to any of claims 11, 12, 14, 18 or 19, characterized in that the target cells is transfected, transformed and/or infected with a nucleic acid according to claim 9 and/or a vector according to claim 10.
22. Method for producing a target cell according to claim 20 or 21, characterized in that the target cell is a B cell, a macrophage, a dendritic cell, an embryonic

cell, a fibroblast, a B16F10, a B6, a C3, an EL4, a RMA or a RMA-S cell.

23. Method according to claim 18 or 19, characterized in that instead of step a) the following step a") is carried out:

a") production and preparation of samples containing T cells and subsequent culturing.

24. Assay system for in vitro detection of the activation of T cells, comprising:

a) at least one T-cell epitope according to any of claims 1-4, at least one compound according to any of claims 5-8, at least one vector according to claim 10, at least one cell according to any of claims 11-14, and/or at least one complex according to any of claims 15-17, and

b) effector cells of the immune system, preferably T cells, in particular cytotoxic T cells or T helper cells.

25. Use of at least one T-cell epitope according to any of claims 1-4 at least one compound according to any of claims 5-8, at least one vector according to claim 10, at least one cell according to any of claims 11-14, and/or at least one complex according to any of claims 15-17 for causing or detecting an immune response.

26. Medicament or diagnostic agent, comprising at least one compound according to any of claims 5-8, at least one vector according to claim 10, at least one cell according to any of claims 11-14, and/or at least one

complex according to any of claims 15-17 and, if necessary, a pharmaceutically acceptable carrier.

27. Medicament or diagnostic agent according to claim 26, characterized in that at least one compound according to any of claims 5-8, at least one vector according to claim 10, at least one cell according to any of claims 11-14, and/or at least one complex according to any of claims 15-17 is present in solution, bound to a solid matrix and/or mixed with an adjuvant.

add
ai